

REMARKS

Applicants request reconsideration of the present application in view of the foregoing claim amendments and the remarks that follow.

Interview summary

Applicants thank Examiner's Cornet and Fetterolf for extending the courtesy of a telephone interview on June 9, 2010. As stated on page two (2) of the interview summary of record, the interview focused on understanding the PTO's interpretation of the claimed invention. In particular, the Examiners stated that phrase "diagnostic composition **comprising** microspheres..." would include magnetite containing microspheres. Supervisory Examiner Fetterolf suggested amending the claim to recite the closed transitional phrase "consisting of."

Applicants do not agree with the Examiners' interpretation of the claimed invention particularly in light of claim language indicating "microspheres consisting of." Applicants have amended claim 8 to delete the term "comprising" solely for the purpose of advancing prosecution. Applicants maintain that while the claimed diagnostic method is directed to administration microspheres consisting of a bio-degradable polymer and having a diameter of about 0.1-10 microns, that additional known components of a lavage, such as buffers, stabilizers, etc., may be administered to the subject with the microspheres, and such components are within the scope of the claimed invention.

Based on the commentary on page 2 of the Interview Summary, Applicants believe this amendment should overcome the prior art rejection of record. Accordingly, after entry of these amendments and in view of the remarks presented below, Applicants believe that the present application is in condition for allowance and await an indication from the PTO to this effect.

Status of the claims

Applicants have amended claim 8 to recite a diagnostic method for detecting pulmonary aspiration or gastroesophageal reflux comprising orally administering to a subject microspheres consisting of a bio-degradable polymer. Support for this amendment can be found throughout the specification and particularly in paragraphs [0007], [0013] and [0014] of publication No. 2005/0214216. Claims 1-7 were previously cancelled and claim 14 is withdrawn. Claims 8-13 are currently pending and are represented for consideration.

Claim Rejections – 35 U.S.C. § 103

Claims 8-13 remain rejected under 35 U.S.C. § 103(a) as unpatentable over “Charcoal is a Sensitive, Specific, and stable Marker for the Diagnostic of Aspiration in Hamsters,” Pediatric Research, March 2002, pp. 397-401, Vol. 51, No. 3, Avital *et. al.*, in view of Assessment of Biodegradability of polymeric Microspheres *in vivo*: Poly(DL-lactic acid), and poly(L-lactic acid) and poly(DL-lactide-co-glycolide) microspheres, Arch. Pharm. Res. Vol. 16, No. 4, pp. 312-317, 1193, Joon *et al.* Applicants respectfully traverse.

Independent claim 8 is directed to a method for detecting pulmonary aspiration or gastroesophageal reflux. Specifically, claim 8 is amended to recite performing the inventive diagnostic method by orally administering to a subject microspheres consisting of a biodegradable polymer and detecting the presence of the biodegradable microspheres within alveolar macrophages obtained by bronchoalveolar lavage.

As described in the specification, the claimed method provides a safe biodegradable marker for detecting pulmonary aspiration or gastroesophageal reflux. See para [0007]. Example 1 teaches the synthesis of biodegradable polylactic acid microspheres, their instillation in the trachea and detection of these microspheres within alveolar macrophages in bronchoalveolar lavage (BAL). The skilled artisan would have readily understood that no additional components are present in the biodegradable microspheres used in the inventive method. Neither Avital nor Joon teach or suggest the claimed diagnostic method.

As acknowledged by the PTO, Avital teaches the use of charcoal as a marker for detecting aspiration in hamsters. Avital teaches identification of charcoal alveolar macrophages (ChAM), in bronchoalveolar lavage (BAL) as a metric for the diagnosis of pulmonary aspiration. However, Avital cautions against the use of this marker in humans. This is because of the ‘increase in total BAL cells found 3 mo[nths] after a single milk-charcoal instillation.’ Avital at page 400, right column. Avital further states that this hypercellularity in BAL may be due to the residence of large charcoal pieces in lung tissue for extended periods of time which cause charcoal pieces to “behave as foreign bodies.” *Id.*, para bridging page 400 and 401.

Moreover, the PTO has acknowledged that charcoal is not a safe marker for detecting aspiration or gastroesophageal reflux in a human and cites Joon to teach bio-degradable microspheres and remedy the deficiencies in Avital.

However, it is not possible to arrive at the claimed diagnostic method based on the combined teachings of Joon and Avital.

Joon is focused on the kinetics of biodegradation of polymeric microspheres *in vivo*. To evaluate the rate of biodegradation *in vivo*, Joon requires a method that would simplify tracing and handling of the microspheres in living systems. More particularly, Joon teaches incorporating magnetite as a tracer for detecting microspheres in the body. See Joon at page 312, left column. Nowhere, does Joon teach or suggest the use of biodegradable microspheres that are devoid of magnetite. Moreover, Joon teaches homogenization of the lung tissue to isolate and recover the polymeric microspheres prior to analyzing the extent of their degradation *in vivo*. That is, Joon's method requires animal sacrifice and would not be regarded as suitable for humans.

The Supreme Court recently explained that a *prima facie* case of obviousness requires all elements of a claim to be in the prior art. In *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), the Court stated that the proper question for evaluating obviousness is "whether there was an apparent reason to combine the known elements in the fashion claimed." *KSR*, 127 S.Ct. at 1741.

Here, neither Avital nor Joon disclose a diagnostic method that comprises orally administering microspheres consisting of a biodegradable polymer and their detection in alveolar macrophages in BAL as claimed. Avital teaches the use of charcoal as a marker for aspiration and Joon teaches magnetite as a tracer for microspheres *in vivo*. Contrary to the PTO's statements, the skilled artisan would not have been motivated to modify Joon's microspheres so as to remove magnetite, because such a modification would change the principle of operation of Joon's invention, that is, removing magnetite would have prevented Joon from tracing and handling the microspheres needed to evaluate the extent of degradation *in vivo*.

As stated in MPEP § 2143.01(VI):

"if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious."
[Emphasis added].

As stated above, Joon specifically adds magnetite to facilitate tracking and handling of the biodegradable microspheres using an applied magnetic field, and removing magnetite from the microspheres would prevent such tracking *in vivo*. The foregoing remarks alone compel the conclusion that the PTO has failed to make a case for *prima facie* obviousness.

Furthermore, even it is assumed *arguendo* that Joon's microspheres could be substituted for the charcoal particle used in Avital's method, the modified method would still differ from the method of claim 8. These remarks lead to the conclusion that the inventive methodology is patentable over the combined teachings of the cited art. Accordingly, claim 8 and the claims that depend therefrom are patentable and Applicants respectfully request the PTO to withdraw the obviousness rejection.

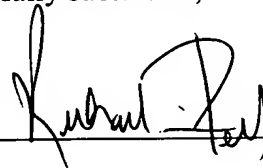
CONCLUSION

Applicants believe that the present application is now in condition for allowance and requests the PTO to provide an early indication to this effect. The Examiner is invited to contact the undersigned if any issues warranting further discussion remain.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, then the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

By



Richard Peet
Attorney for Applicant
Registration No. 35,792

Date June 21, 2010 (Monday)

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 295-4620
Facsimile: (202) 672-5399